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(54) Title: HUMAN SECRETED PROTEINS

(57) Abstract: The present invention relates to human secreted polypeptides, and isolated nucleic acid molecules encoding said polypeptides, useful for diagnosing and treating immune disorders and diseases. Antibodies that bind these polypeptides are also encompassed by the present invention. Also encompassed by the invention are vectors, host cells, and recombinant and synthetic methods for producing said polynucleotides, polypeptides, and/or antibodies. The invention further encompasses screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further encompasses methods and compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.



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		Met-1 to Cys-12.	Met-1 to Cys-12.	_	Ala-18 to Gly-38,	Pro-56 to Pro-79,	Pro-96 to Ala-113,	Gln-116 to Gly-128.	_	Ala-76 to Lys-111.	Trp-29 to Gly-42, Gly-46 to His-51.		Val-54 to Asp-59.		Val-54 to Asp-59.	Thr-26 to Asn-39.	Pro-57 to Pro-64.	Lys-1 to Gly-8.	Lys-47 to Pro-58.	Met-1 to Cys-7,	Gln-45 to Gly-61,	Gln-77 to Thr-93,	Arg-113 to Arg-118,	Ser-135 to Glu-147, Gln-155 to Ala-161.	+-		Thr-36 to Leu-41.	Pro-30 to Ala-35.
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241	242	243							244		245	246	247			248			249	250					251	252	253	254

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				Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):387-396 (1997); and flenderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available the than the ATCC. Evernlary human mast calls that may be used according to these assays.
				(e.g., unough the ATCC). Exemplary infinal mass constituted that the established from the peripheral include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.
243	HHSGW69	1150	Production of	IL-10 FIMAT. Assays for immunomodulatory proteins produced by activated T cells, B cells, and
			downregulati	expression of cytokines are well known in the art and may be used or routinely modified to assess the
			on of immine	ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation regulate inflammatory activities and modulate immune cell
			responses	function and cytokine production. Exemplary assays that test for immunomodulatory proteins evaluate
				the production of cytokines, such as IL-10, and the downmodulation of immune responses. Such assays
				that may be used or routinely modified to test immunomodulatory activity of polypeptides of the
				invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed
	-			in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical
				approach Chapter 0:138-160 (2000); and Koning et al., Cytokine 9(0):42/450 (1997), the contents of
	•			each of which are herein incorporated by reference in its entirety. Human I cells that may be used
				according to these assays may be isolated using techniques disclosed herein or otherwise known in the
				art. Human I cells are primary human lymphocytes that mature in the thymus and express a 1 cell
				receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be
				preactivated to enhance responsiveness to immunomodulatory factors.
244	HHTLF25	1151	Production of	IL-10 FMAT. Assays for immunomodulatory proteins produced by activated T cells, B cells, and
			L-10 and	monocytes that exhibit anti-inflammatory activity and downregulate monocyte/macrophage function and
			downregulati	expression of cytokines are well known in the art and may be used or routinely modified to assess the
			on of	ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the
			immune	invention) to mediate immunomodulation, regulate inflammatory activities, and modulate immune cell
			responses	function and cytokine production. Exemplary assays that test for immunomodulatory proteins evaluate
				the production of cytokines, such as IL-10, and the downmodulation of immune responses. Such assays
				that may be used or routinely modified to test immunomodulatory activity of polypeptides of the
				invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed
				in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rówland et al., "Lymphocytes: a practical
				approach" Chapter 6:138-160 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of
				each of which are herein incorporated by reference in its entirety. Human T cells that may be used

according to these assays may be isolated using techniques disclosed herein or otherwise known in the act. Human T cells are primary human lymphocyes that mature in the thymus and express a T cell receptor and CD3, CD3, CD3. These cells mediate humoral or cell-mediated immunity and may be used or toutinely modified to assess the ability of polypeptides of the invention of including antibodies and activation of gaonists or antagonists of the invention (including agonists of the invention (including agonists of the invention (including agonists of the invention include. In coample agonists of the invention include or including to mindlo activation and antibodies of the invention include. In coample assays such as disclosed and/or cited in Robinson. DS; et al., "The Z-pokchas in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and COM, et al., "The Part type 2 cell directed therepy for ashmir* Pharmacology & Thereputies; 88: 187-196 (2000), the contents of each of which have herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include TT2 cells. Lt. 0. Secreted from Th2 cells may be measured as a marker of TT2 cell and as a class of T cells that secrete LL. LL. 0. LL.3. LL. and LL. 0. LL.3. LL. and L. Polarizing conditions using peripheral blood lymphocytes is loadered from condition of MCP-1 RMAT. Assays for immunomodulatory proteins and activation of That cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes and activation of for a seass that and activation of monocytes and activation of many peripheral blood lymphocytes and activation of MCP-1 RMAT. Assays for immunomodulatory proteins that are produced by a large creating manual agonists or antagonists of the invention in mediate immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention of monocytes and T cells. Such assays that may be used or routinely modi
HJABX3
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	339	218	200	1301	807	1298 828	762	65	114 536	114		787	976	613	967 928	619	780 582	474	612
	326	45	180	132	628	819 130	1	592	7 378	7	3/0	707	191	542	191 338	548	730 529	142	463
	72% 83%	100%	26%	%001	36.3	%66 %86	100%	%66	94%	94%	70.70	59% 52%	74%	122	74% 30%	77	100%	91%	%86
8.1 AAH008 28	ововове		Q9D1N2	Q96AP7	PF00047	Q96AP7	Q99LX9	Q9H7P4	Q96FV2	Q96FV2		Q9P1J1	Q9HBW1	PF00560	Q9НВW1	PF00560	095325	Q9UMT3	070277
sapiens]	(Q9BQB6) UNKNOWN (PROTEIN FOR MGC:11276) (PROTEIN FOR IMAGE:3455200).		(Q9D1N2) 1110002J19RIK PROTEIN.	(Q96AP7) Hypothetical 41.2 kDa protein.	PFAM: Immunoglobulin domain	(Q96AP7) Hypothetical 41.2 kDa protein.	(Q99LX9) SIMILAR TO SINGLE-STRANDED-DNA-BINDING PROTEIN.	(Q9H7P4) FLJ00024 PROTEIN (FRAGMENT).	(Q96FV2) Unknown (protein for IMAGE:3945715) (Fragment).	(Q96FV2) Unknown (protein for IMAGE:3945715) (Fragment).		(Q9P1J1) PRO1546.	(Q9HBW1) Brain tumor associated protein NAG14.	PFAM: Leucine Rich Repeat	(Q9HBW1) Brain tumor associated protein NAG14.	PFAM: Leucine Rich Repeat	(095325) PROTEASOME SUBUNIT P58.	(Q9UMT3) KILLER ACTIVATING RECEPTOR ASSOCIATED PROTEIN, ISOFORM B.	(070277) RING FINGER PROTEIN.
	WUblastx.64		WUblastx.64	WUblastx.64	HMMER 2.1.1	WUblastx.64	WUblastx.64	WUblastx.64	WUblastx.64	WUblastx.64		WUblastx.64	WUblastx.64	HMMER 2.1.1	WUblastx.64	HMMER 2.1.1	WUblastx.64	WUblastx.64	WUblastx.64
	708		241	242	709		244	245	246	712		248	250	713		714	253	254	255
	535730		905849	865581	691402		411470	1127491	662329	383547		554613	1299927	753270		560969	1031514	461438	487807
	HHEPU04		HIHFEC49	HHFGR93	HHFGR93		HHFHR32	HHFOJ29	ннссм76	нносм76		HHGDW4	HHPGO40	HHPGO40		HHPGO40	69MDSHH	HHTLF25	HJABX32

					1 7
		_			AL137557.1, AF207829.1,
				_	AL136799.1, AL050138.1, AL389982.1, AK026959.1,
-					AL133557.1, AL359601.1, AK026927.1, BC006195.1,
					AK027868.1, AB056768.1, AL133093.1, BC006807.1,
					, AL096744.1, AB051158.1, AK026532.1, AK025209.1,
					AL133565.1, BC008070.1, AB060826.1, AK026542.1,
					AB060863.1, AL080124.1, AL136768.1
					X82434.1, AK027164.1, AK026583.1, AB048954.1, A
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					AF260566.1, AL353940.1, BC008899.1, AK000618.1,
					AK025772.1, AB055315.1, AL049464.1, AL122123.1,
					AB056421.1, AF091084.1, AB060852.1,
			•		BC008485.1,
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					U91329.1, AJ
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					AL137538.1,
-					AL512761.1, X72889.1, AK025524.1, AL136843.1, AL133113.1,
					AL137648.1,
					AL110197.1, AL359622.1, BC006164.1, AB060883.1, AF271350.1, BC008893.1,
					AK026526.1, BC001349.1, AC019095, AC019095.
HHTLF25	254	461438	1 - 683	15 - 697	AA481924, BF343628, AI276798, BE858514, BF915546, BG058647, BF917552, AI299346,
					N41026, BF914451, AA989053, W60864, BF915075, AI423526, BF106006, AI289858, AA746220,
					BF915128, AI306602, AW015647, AA633118, AI207255, BF913974, AI301688, W92376,
					AI139176, AA971275, AA480109, H12338, BF912934, AA865668, BF901361, F30553, AW973896,
					AA991168, AI302882, BF915115, AA729941, AA627378, AA865651, AW607348, H39980,
		· · ·			AA729534, T55959, T57206, AW607175, W60940, BE155729, A1880682, AW383808, BG058709,
					AW383055, AW383057, BE154544, AW383016, AW383047, AW383871, AW383051, BF901355,
		•			AW383000, AI919456, BE154555, AW383784, BF914191, F32872, AI017727, AA974881,
					BE154538, AW383009, BF092099, AI243983, AA991170, R49835, R49793, AA318120, BF893642,
					W74783, AW382999, AV712713, AW579628, AW382994, H12392, AW372144, AW372157,
					AW383836, T52100, AW372154, AW383822, AW383837, AW579627, AW383817, AW372166,
		-			BF881098, AW382997, D20493, AW372161, AW383865, AA918360, N47127, AW579992,
					AA93/6/U, AW5/9601, AW5/9988, AU0/6484, AI2452/3, BF831139, AA664094, AA8/8598,

					AA865673, AI807718, AA937805, BF350664, AI525220, AD000833.1, AF019563.1, AF019562.1, AJ010098.1, AD000864.1, X78928.1, AF072845. 1.
HJABX32	255	487807	1 - 1047	15 - 1061	BE385796, AL048522, AA114843, AV723581, AA114842, AA565480, AA310353, D80486, D60174, BF953264, D60503, D59975, BF950356, BF950358, D60175, AW612691, AI972034, BE677654, D81110, AI017365, N71311, AA248844, AW953422, D80968, D60623, H22225, AI439412, N71362, C15057, AA907114, BF953271, A1783844, AI086417, BE254805, AI088382, AI813642, AI971901, AL122053.1, AF220022.1, AF220021.1, AF045239. 1.
HJACA79	256	562729	1 - 873	15 - 887	BE34841, BE644740, Ai912665, AA310811, AW504485, AV763026, AV763058, AW502796, AW500029, BE207631, AJ732151, AL079734, AV711465, AW327624, AJ357823, AA469327, NA2040, AW970877, BF681619, AU152561, AW148507, AI040051, AW302909, AL188390, AL654285, AV759632, AW855803, AW855730, AJ75113, AW190505, AV760918, AJ755202, AL66448, AV769181, AA613624, AU37897, AL761756, AA602557, AA491960, BE062476, BE066448, AV769151, AA613624, AU37897, AL1071941, AW571499, AI755037, AJ366902, AA809546, AL048135, AA877992, AW468003, AL047756, AA602597, AL120959, AW274072, AC068799.14, AC009087.4, AC003041.1, AC006441.13, AC005874.3, AF134471.1, AC005701.1, AL049820.23, AP001717.1, AL049715.25, AC02392.4, AL034549.19, AC006165.1, AC005701.5, Z85986.1, AL138960.16, AC008569.6, AC007052.4, AL035690.10, AC012627.4, AC002531.1, AC006285.11, AC005520.2, AL162615.13, AC006285.11, AC005252.1, AC0055377.2, AL136909.14, AC005250.2, AL13609.4, AL034418.5, AL3916445, AC007899.3, AC004859.2, AL136308.4, AL138502.38, AC007374.6, AC007956.5, AL109627.18, AL353812.13, AC004929.2, AL356257.14, AC007374.6, AC007956.5, AL106027.18, AL353812.13, AC004929.2, AL356257.14, AC007374.6, AC007956.3, AC006116.1, AL31329.12, AC007318.4, AC003347.2, AC007360.3, AC006116.1, AL31329.12, AC007318.4, AC003344.5, AC006010.2, AL13629.2, AL356257.14, AC007374.6, AC007956.3, AC006116.1, AL31329.12, AC007318.4, AC009144.5, AC007960.2, AL391239.1, AC003383.1, AL1313299.2, AL39120.9, AC006010.2, AL139129.12, AC009983.1, AC006010.2, AL139129.12, AC009983.2, AL139100.9, AC006010.2, AL09646.19, AC006077.1, AL391259.15, AC004983.2, AL139100.9, AC01448.3, AC004983.2, AL19903357.2, AC011443.6, AC01448.3, AC004983.2, AL19903357.2, AC011443.6, AC011443.6, AC011443.6, AC0099983.1, AC01448.3, AC004983.2, AL1990996.1, AC011448.3, AC01448.3, AC004983.2, AL1990996.1, AC011449.6, AC011448.3, AC011448.3, AC004983.2, AL1990996.1, AC011448.3, AC01144
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